REMARKS

Upon entry of this amendment, claims 1-37, 77, 83-94, 97-108,119, and 121-123 will be pending in the application. Claims 1-37, 77, 84-87, 93, 94, 97 and 101-108 were previously withdrawn. Claims 38-76, 78-82, 96, 109-117 and 124-130 were previously cancelled.

Claims 118 and 120 are presently cancelled without prejudice in order to further prosecution. Applicants reserve the right to pursue the subject matter of the cancelled claims in one or more subsequent patent applications. Claim 121 is currently amended solely to overcome a claim objection and Applicants submit that the amended claim is of equivalent scope and presents no new issues. The Examiner is requested to enter the present amendment as cancellation of Claims 118 and 120 and the amendment of Claim 121 present no new issues and further place the claims in better form for appeal, as per 37 C.F.R. § 1.116(b)(1) & (2).

The Examiner is requested to reconsider and withdraw the rejections in view of the amendments and remarks contained herein.

EXAMINER'S INTERVIEW

Applicants acknowledge and appreciate the courtesy afforded by Examiner Bristol in an interview conducted on July 23, 2009 with Applicants' representative Fernando Alberdi. Applicants also acknowledge the Interview Summary issued July 28, 2009, providing a summary of the subject matter discussed in the interview. Applicants thank the Examiner for her careful analysis of the meanings of the terms "at least", "preferably" and

"optionally" as recited in Herman a reference of record with respect to the rejection under 35 U.S.C. § 102(e) and for discussing the same with her conferees.

1. Rejection Under 35 U.S.C. § 112

Claims 118 and 120 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking an enabling disclosure for the reasons of record as set forth in the Office Actions of 11/7/06, 7/19/07 and 4/10/08 and 11/18/08.

Cancellation of Claims 118 and 120 by the present amendment renders the rejection moot. Accordingly, withdrawal of the rejection is requested.

2. Rejection Under 35 U.S.C. § 102

Claims 83, 88-92, 95, 98-100, and 118-123 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Herman (U.S. Pub. No. 2005/0069549, published March 31, 2005, filed January 14, 2003). This rejection is respectfully traversed.

The present claims are novel over Herman as the reference fails to provide all of the claimed features as recited in the present claims. See *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (each and every element in the claim must be present in the reference for the claim to be anticipated). In particular, Herman fails to provide a nucleic acid, encoding a monomer unit of a recombinant antibody-based dimeric molecule, which has targeting and antigenic units separated by a dimerization motif and which lacks a CH2 domain. Herman further fails to provide for a dimerization motif that includes an Ig hinge region

(providing dimerization via disulfide bridging) and a Cγ3 domain (providing dimerization via hydrophobic interactions).

The rejection, originally set forth in the Office Action dated November 18, 2008, erroneously assumes that Herman anticipates the present claims based solely on the fact that various features of the present claims appear to be located at various points throughout the reference. This is an incorrect approach. Anticipation requires disclosure of all the claimed features as arranged in the claim – there must be an instance, description, or embodiment that expressly accounts for all aspects of Applicants' claim as arranged in the claim. One cannot pick and choose features from different embodiments in Herman to reconstruct the present claims under 35 U.S.C. § 102. Herman must expressly disclose the particular combination of features since anticipation requires a reference to disclose all elements as they are laid out in Applicants' claims. The rejection, as quoted on pages 9-10 of the Office Action dated May 6, 2009, simply runs through the Herman disclosure as a laundry list of parts without accounting for and identifying any direction or guidance on how to assemble particular parts in the exact fashion as claimed. Applicants submit that the rejection has failed to explicitly identify any example or description in Herman where all of Applicants claimed features are arranged as found in the present claims.

Instead, the rejection appears to be predicated on a "target ligand," as per Herman, that merely sums the whole of the disclosure into a single "multispecific ligand," discounting the necessary exchange of certain features, incompatibilities of certain features, redundancies, and likely inoperability of certain combinations. The rejection's incorrect approach is illustrated on page 11 of the Office Action dated May 6,

2009, where it is said that "Herman teaches all of the elements for designing such a construct." The issue in anticipation is not whether all the elements are available for designing the present claims; the issue is whether the reference actually discloses all the elements as arranged in the present claims. For example, disclosure of all 20 conventional amino acids does not amount to disclosure of all polypeptides composed of these amino acids.

It is alleged that Herman discloses nucleic acids and vectors encoding a multispecific ligand that reads on Applicants' nucleic acid encoding a monomer unit of a recombinant antibody-based dimeric molecule. Herman paragraph [0424] describes DNA sequences can encode polypeptides sufficient to constitute a multispecific ligand. The multispecific ligand can include first and second ligand binding moieties. Herman abstract. The construct includes an Fc portion or partial Fc portion (e.g., CH2 or minibody-CH3) or weighted Fc, or IgG. Herman paragraph [0069]. The multispecific ligand may also comprise an Fc portion and a hinge portion. Herman paragraph [0116]. The multispecific ligand may have a ligand which binds to a specific MHC peptide complex and a reduced affinity ligand which binds to a ligand on an APC. Herman paragraph [0137]. This collection of features does not amount to the present claims.

Applicants and the Examiner agree that the present claims are drawn to a "nucleic acid encoding a monomer comprising the targeting unit–dimerization motif (Ig hinge and Cγ3)–antigenic unit or antigenic unit–dimerization motif (Ig hinge and Cγ3)–targeting unit." Office Action dated May 6, 2009, page 11. Applicants, however, disagree with the selection and arrangement of particular elements from the Herman disclosure. Paragraph [0345] of Herman allegedly directs construction of a multispecific

ligand having all the features and arrangement of the present claims, according to the excerpt reproduced below:

> For example in a preferred embodiment the bispecific antibody comprises two dAb components comprising linked via a linker (see above) and having at least at least [sic] part of a constant region for fusion for example to a toxin (e.g. at least a partial hinge region, and preferably also at least a partial CH2 domain (optionally also at least a partial CH3 domain).

The Applicants' representative and the Examiner discussed at length during the interview what Herman teaches in this paragraph. This ambiguous sentence does not direct the construction of features as arranged in the present claims. It is the Examiner's position that Herman has taught all of the underlying features of Claim 83 or at least has suggested all of the features of Claim 83. In particular, it is the Examiner's position that Herman conceivably suggests a construct having all of the claim elements of Claim 83, based on the teaching: "at least a partial hinge region, and preferably also at least a partial CH2 domain (optionally also at least a partial CH3 domain)"

Applicants respectfully submit that Herman fails to teach or suggest the claimed features of Applicants' invention. The cited portions of Herman do not even mention a molecule including a targeting unit and an antigenic unit separated by a dimerization motif. This is because "at least a partial CH3 domain" is not necessarily a Cγ3 domain and it need not be sufficiently hydrophobic so as to provide for hydrophobic interactions with an identical monomer and because "at least a partial hinge region" need not include the cysteine residues necessary for disulfide bridging. The "at least a partial CH3 domain" does not disclose the presently claimed Cγ3 domain, in particular, as Cγ3 is but one out of five possibilities: Cα3, Cδ3, Cμ3, Cε3, and Cγ3; i.e., the carboxy terminal constant (C) region domains of an antibody chain is defined by multiple

isotypes of IgH chains (mu, delta, gamma, epsilon, and alpha, which define IgM, IgD, IgG, IgE, and IgA, respectively). Furthermore, Herman fails to teach or suggest using a partial Fc portion or CH3 derived from an IgG3 molecule at all. What is more, the present claims expressly require the CH2 domain to be absent, while the Herman bispecific antibody includes "preferably also at least a partial CH2 domain." Thus, it is not clear when all or some of the CH2 domain is present in Herman. Applicants appreciate the Examiner's careful review of the vagueness and uncertainty provided by paragraph [0345] of Herman.

In any event, Herman fails to teach a "dimerization motif comprising an Ig hinge region and a Cγ3 domain of each monomer unit ... and wherein said monomer units each lack a CH2 domain" as presently recited in Claim 83 and claims dependent thereon. In fact, Applicants read Herman's paragraph [0345] as disclosing a bispecific construct that includes at least a partial hinge region and also at least a partial CH2 domain and further also at least a partial CH3 domain. To exclude the CH2 domain and only include a Cγ3 domain part does not seem to be specifically taught at all as required by MPEP §2131 or in the alternative, suggested as would be required under an obviousness based rejection under §103(a) (MPEP §2143.03). The presence of the partial CH3 domain is not indicated as an alternative to the presence of the CH2 domain. This is a logical conclusion – when it is preferred that the at least partial CH2 domain is present, and then in a parenthetic sentence mentioned to be optional that the at least partial CH3 domain also is present, it does not seem reasonable to interpret this as teaching of presence of a complete CH3 domain (and moreover a Cγ3 domain) but complete absence of the CH2 domain.

Further, it is alleged that the cited construct in Herman can be expressed from a nucleic acid. This is far from certain, however, as there is no disclosure in Herman of the nature of the linker between the two dAb components, especially not a linker which will ensure that the two dAb components can bind to different epitopes (which they must do, since Herman relates to bispecific molecules).

In sum, there is neither an explicit nor an implicit disclosure in Herman of the presently claimed nucleic acid. There is not even a disclosure of the expression product of a nucleic acid and certainly not of an expression product which includes all the features of the monomer unit defined in Claim 83. Specifically, Applicants submit that nowhere does the Herman reference provide an example or a suggestion of a nucleic acid, encoding a monomer unit of a recombinant antibody-based dimeric molecule, which has targeting and antigenic units separated by a dimerization motif, which lacks a CH2 domain, and where the dimerization motif includes an Ig hinge region (providing dimerization via disulfide bridging) and a Cy3 domain (providing dimerization via hydrophobic interactions). Accordingly, reconsideration of the claims and withdrawal of the rejection are requested.

3. CLAIM OBJECTIONS

Claims 120 and 121 are objected to because they reference two sets of claims drawn to different features (MPEP 608.01(n)).

Claim 120 is cancelled rendering the rejection moot as applied thereto.

Claim 121 is amended to indicate that the composition comprises "a nucleic acid according to Claim 83 or a vector comprising the nucleic acid according to Claim 83, in

combination with a physiologically acceptable diluent or carrier." As such, the claim references only Claim 83. Withdrawal of the objection is requested.

4. Conclusion

It is believed that all of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider and withdraw all presently outstanding rejections. It is believed that a full and complete response has been made to the outstanding Office Action and the present application is in condition for allowance. Thus, prompt and favorable consideration of this amendment is respectfully requested. If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (248) 641-1600.

Respectfully submitted,

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By: _____

Robert M. Siminski, Reg. No. 36,007
William A. Ziehler PhD, Reg. No. 61,415
Fernando Alberdi PhD, Reg. No. 62,688

HARNESS, DICKEY & PIERCE, P.L.C.
P.O. Box 828
Bloomfield Hills, Michigan 48303
(248) 641-1600

RMS//FEA/WAZ/akb